DETAILED ACTION

Specification

The instant specification is not in compliance with the sequence rules, 37 CFR 1.821-1.825. Figures 1 and 2 disclose sequences that are not included in the sequence listing. These sequences should be referenced by appropriate sequence identifiers in the specification or in the figure itself. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

SEQ ID NOS: 2 and 4 are disclosed as being novel fibulin-like polypeptides. The specification does not disclose any significant homology to any fibulin protein that has been disclosed and characterized in the prior art. A sequence search of SEQ ID NOS: 2 and 4 did not reveal any significant homology to any fibulin protein disclosed and characterized in the prior art. (See for example prior art to Argrave et al., Tran et al., and Pan et al. for fibulin-1.) Although Figure 2 aligns SEQ ID NO: 2 (designated SCS0007) with AK056571 (corresponding to SEQ ID NO: 2652 of Isogai et al., U.S. Patent No. 6,979,557), the protein of Isogai et al. itself is disclosed as being only weakly similar to fibulin-1, isoform A precursor. Isogai et al. does not

determine any biological activity for this protein. The Genbank entry for XP_166226 (see Figure 2) provides no citation or reference for the source of this sequence. No verified biological activity or use for this protein is provided. Searching Genbank for HCP50656.1 (see Figure 1) did not reveal a verified biological activity or use for this protein. FLJ32009 appears to correspond to a protein characterized by Lian et al. (2003). This reference was published **after** the priority date claimed by applicant. The protein disclosed by Lian et al. is not identified as a fibulin-like protein or as having calcium binding EGF domains. The alignment of SEQ ID NO: 2 to the sequences in Figure 1 shows significant sequence variation.

With respect to variants and fragments that bind calcium ions (see at least claims 57, 60, 61, 63, 66, and 67), the specification does not identify those amino acids or domains responsible for calcium binding activity. As such, one of ordinary skill in the art would not know which areas of SEQ ID NO: 2 or 4 could be mutated and retain this activity. In fact, the specification does not demonstrate that the full length sequences of SEQ ID NOS: 2 and 4 bind calcium ions themselves.

With respect to claim 62, the specification does not disclose the chemical structure of any peptide mimetics. The specification does not disclose the structure or function that must be present to meet the limitatons of this claim. It is not known what biological activity is required by this claim.

With respect to claims 63-67, the specification does not provide any examples of administering SEQ ID NOS: 2 or 4 to any individual with the recited diseases or conditions and showing any positive effect. The specification and prior art of record do not disclose or establish that SEQ ID NOS: 2 or 4 or any fibulin-like protein can be used to treat any or all of the recited

diseases or conditions. There are no proteins with established biological activities or comparable methods of treatment disclosed by which one of ordinary skill in the art would have been able to extrapolate to the claimed methods of treatment.

The specification does not establish a biological activity for SEQ ID NOS: 2 and 4. In the absence of such an activity, one of ordinary skill in the art would not have known how to use these proteins. The claimed methods of treatment are an invitation to experiment in view of the lack of guidance, absence of examples, and lack of knowledge in the prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 57 and 60-62 are rejected under 35 U.S.C. 102(e) as being anticipated by Isogai et al. (U.S. Patent No. 6,979,557).

Isogai et al. discloses SEQ ID NO: 2652. This protein is disclosed as being related to fibulin-1 isoform A. See at least column 37, line 47; columns 121-124, particularly column 123, line 63; and column 213, lines 7-8. This protein has greater than 88% identity (i.e. no more than 15% of the amino acid residues in the sequence are changed) to instant SEQ ID NOS: 2 and 4. The polypeptide of Isogai et al. comprises fragments of SEQ ID NOS: 2 and 4. It can be considered a peptide mimetic as recited in claim 62. See sequence alignments set forth below.

The instant application premises the activity of SEQ ID NOS: 2 and 4 based on the homology to the sequence of Isogai et al. See at least instant Figure 2.

The prior art attributes the calcium binding activity of fibulin to epidermal growth factor domains (EGF domains) 5-9. (See for example Tran et al.) The sequence of Isogai et al. contains sequence corresponding to some of these domains. Absent evidence to the contrary, the protein of Isogai et al. would bind calcium ions thereby meeting the limitations of the claims. Should applicant provide evidence that calcium ions are not bound by the sequence of Isogai et al. this will be considered further evidence that the claims are not enabled for fragments and variants that bind calcium ions.

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Alignment of instant SEQ ID NO: 2 with SEQ ID NO: 2652

US-10-094-749-2652
; Sequence 2652, Application US/10094749
; Patent No. 6979557
; GENERAL INFORMATION:
;  APPLICANT: ISOGAI, TAKAO
; SEQ ID NO 2652
;   LENGTH: 955
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-094-749-2652

  Query Match             88.3%;  Score 4105;  DB 2;  Length 955;
  Best Local Similarity   77.8%;  Pred. No. 2.9e-239;
  Matches  752;  Conservative    6;  Mismatches   28;  Indels  180;  Gaps
10;

Qy          1 MWAGLLLRAACVALLLPGAPARGYTGRKPPGHFAAERRRLGPHVCLSGFGSGCCPGWAPS 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MWAGLLLRAACVALLLPGAPARGYTGRKPPGHFAAERRRLGPHVCLSGFGSGCCPGWAPS 60

Qy         61 MGGGHCTLPLCSFGCGSGICIAPNVCSCQDGEQGATCPETHGPCGEYGCDLTCNHGGCQE
120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 MGGGHCTLPLCSFGCGSGICIAPNVCSCQDGEQGATCPETHGPCGEYGCDLTCNHGGCQE
120

Qy        121 VARVCPVGFSMTETAVGIRCTDIDECVTSSCEGHCVNTEGGFVCECGPGMQLSADRHSCQ
180
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                ||||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 VARVCPVGFSMTEAAVGIRCTDIDECVTSSCEGHCVNTEGGFVCECGPGMQLSADRHSCQ
180

Qy        181 DTDECLGTPCQQRCKNSIGSYKCSCRTGFHLHGNRHSCVDVNECRRPLERRVCHHSCHNT
240

                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 DTDECLGTPCQQRCKNSIGSYKCSCRTGFHLHGNRHSCVDVNECRRPLERRVCHHSCHNT
240

Qy        241 VGSFLCTCRPGFRLRADRVSCEG--------------------------------AL----
265

                |||||||||||||||||||||                                  ||
Db        241 VGSFLCTCRPGFRLRADRVSCEAFPKAVLAPSAILQPRQHPSKMLLLLPEAGRPALSPGH
300

Qy        266 SPPDWQQGPLPAG----------------------TW-------------------------
280

                |||    || |||                     |
Db        301 SPPSGAPGP-PAGVRTTRLPSPTPRLPTSSPSAPVWLLSTLLATPVPTASLLGNLRPPSL
359

Qy        281 ------------------------EPCMNQGVAGQSLG-----------------------
294

                                       || : |   :|
Db        360 LQGEVMGTPSSPRGPESPRLAAGPSPCWHLGAMHESRSRWTEPGCSQCWCEDGKVTCEKV
419

Qy        295 ---------VPSA-GARLETCRACF--------------------VSVLLA---------
315

                    :||  |    :|  ||                       | | ||
Db        420 RCEAACSHPIPSRDGGCCPSCTGCFHSGVVRAEGDVFSPPNENCTVCVCLAGNVSCISPE
479

Qy        316 ----RVRPPIKTDCCTCVPVRCYFHGRWYADGAVFSGGGDECTTCVCQNGEVECSFMPCP
371

                 : | :||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        480 CPSGPCQTPPQTDCCTCVPVRCYFHGRWYADGAVFSGGGDECTTCVCQNGEVECSFMPCP
539

Qy        372 ELACPREEWRLGPGQCCFTCQEPTPSTGCSLDDNGVEFPIGQIWSPGDPCELCICQADGS
431

                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        540 ELACPREEWRLGPGQCCFTCQEPTPSTGCSLDDNGVEFPIGQIWSPGDPCELCICQADGS
599

Qy        432 VSCKRTDCVDSCPHPIRIPGQCCPDCSAAGAQRMLSLAGCTYTGRIFYNNETFPSVLDPC
491

                ||||||||||||||||||||||||||          ||||||||||||||||||||||
Db        600 VSCKRTDCVDSCPHPIRIPGQCCPDCS----------AGCTYTGRIFYNNETFPSVLDPC
649

Qy        492 LSCICLLGSVACSPVDCPITCTYPFHPDGECCPVCRDCNYEGRKVANGQVFTLDDEPCTR
551
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        650 LSCICLLGSVACSPVDCPITCTYPFHPDGECCPVCRDCNYEGRKVANGQVFTLDDEPCTR
709

Qy        552 CTCQLGEVSCEKVPCQRACADPALLPGDCCSSCPDSLSLPLEEKQGLSPHGNVAFSKAGRS
611
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        710 CTCQLGEVSCEKVPCQRACADPALLPGDCCSSCPDSLSLPLEEKQGLSPHGNVAFSKAGRS
769

Qy        612 LHGDTEAPVNCSSCPGPPTASPSRPVLHLLQLLLRTNLMKTQTLPTSPAGAHGPHSLALG
671
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        770 LHGDTEAPVNCSSCPGPPTASPSRPVLHLLQLLLRTNLMKTQTLPTSPAGAHGPHSLALG
829

Qy        672 LTATFPGEPGASPRLSPGPSTPPGAPTLPLASPGAPQPPPVTPERSFSASGAQIVSRWPP
731
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        830 LTATFPGEPGASPRLSPGPSTPPGAPTLPLASPGAPQPPPVTPERSFSASGAQIVSRWPP
889

Qy        732 LPGTLLTEASALSMMDPSPSKTPITLLGPRVLSPTTSRLSTALAATTHPGPQQPPVGASR
791
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        890 LPGTLLTEASALSMMDPSPSKTPITLLGPRVLSPTTSRLSTALAATTHPGPQQPPVGASR
949

Qy        792 GEESTM 797
                ||||||
Db        950 GEESTM 955


Alignment of instant SEQ ID NO: 4 with SEQ ID NO: 2652


US-10-094-749-2652
; Sequence 2652, Application US/10094749
; Patent No. 6979557
; GENERAL INFORMATION:
;  APPLICANT: ISOGAI, TAKAO
;    LENGTH: 955
;    TYPE: PRT
;    ORGANISM: Homo sapiens
US-10-094-749-2652

  Query Match             88.1%;  Score 4001;  DB 2;  Length 955;
  Best Local Similarity   77.4%;  Pred. No. 9.2e-233;
  Matches  732;  Conservative    6;  Mismatches   28;  Indels  180;  Gaps
10;

Qy          1 ARGYTGRKPPGHFAAERRRLGPHVCLSGFGSGCCPGWAPSMGGGHCTLPLCSFGCGSGIC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        21 ARGYTGRKPPGHFAAERRRLGPHVCLSGFGSGCCPGWAPSMGGGHCTLPLCSFGCGSGIC 80

Qy        61 IAPNVCSCQDGEQGATCPETHGPCGEYGCDLTCNHGGCQEVARVCPVGFSMTETAVGIRC
120

           ||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||
Db        81 IAPNVCSCQDGEQGATCPETHGPCGEYGCDLTCNHGGCQEVARVCPVGFSMTEAAVGIRC
140

Qy       121 TDIDECVTSSCEGHCVNTEGGFVCECGPGMQLSADRHSCQDTDECLGTPCQQRCKNSIGS
180

           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       141 TDIDECVTSSCEGHCVNTEGGFVCECGPGMQLSADRHSCQDTDECLGTPCQQRCKNSIGS
200

Qy       181 YKCSCRTGFHLHGNRHSCVDVNECRRPLERRVCHHSCHNTVGSFLCTCRPGFRLRADRVS
240

           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       201 YKCSCRTGFHLHGNRHSCVDVNECRRPLERRVCHHSCHNTVGSFLCTCRPGFRLRADRVS
260

Qy       241 CEG--------------------------------AL----SPPDWQQGPLPAG-------
258

           ||                                    ||    |||    || |||
Db       261 CEAFPKAVLAPSAILQPRQHPSKMLLLLPEAGRPALSPGHSPPSGAPGP-PAGVRTTRLP
319

Qy       259 --------------TW-----------------------------------------------
260

                          |
Db       320 SPTPRLPTSSPSAPVWLLSTLLATPVPTASLLGNLRPPSLLQGEVMGTPSSPRGPESPRL
379

Qy       261 ----EPCMNQGVAGQSLG-------------------------------VPSA-GARLET
284

                 || : |   :|                                    :||  |    :
Db       380 AAGPSPCWHLGAMHESRSRWTEPGCSQCWCEDGKVTCEKVRCEAACSHPIPSRDGGCCPS
439

Qy       285 CRACF--------------------VSVLLA-------------RVRPPIKTDCCTCVPV
311

           |  ||                      | | ||               : | :|||||||||
Db       440 CTGCFHSGVVRAEGDVFSPPNENCTVCVCLAGNVSCISPECPSGPCQTPPQTDCCTCVPV
499

Qy       312 RCYFHGRWYADGAVFSGGGDECTTCVCQNGEVECSFMPCPELACPREEWRLGPGQCCFTC
371

           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       500 RCYFHGRWYADGAVFSGGGDECTTCVCQNGEVECSFMPCPELACPREEWRLGPGQCCFTC
559

Qy       372 QEPTPSTGCSLDDNGVEFPIGQIWSPGDPCELCICQADGSVSCKRTDCVDSCPHPIRIPG
431

           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        560 QEPTPSTGCSLDDNGVEFPIGQIWSPGDPCELCICQADGSVSCKRTDCVDSCPHPIRIPG
619

Qy        432 QCCPDCSAAGAQRMLSLAGCTYTGRIFYNNETFPSVLDPCLSCICLLGSVACSPVDCPIT
491
              |||||||           ||||||||||||||||||||||||||||||||||||||||||
Db        620 QCCPDCS----------AGCTYTGRIFYNNETFPSVLDPCLSCICLLGSVACSPVDCPIT
669

Qy        492 CTYPFHPDGECCPVCRDCNYEGRKVANGQVFTLDDEPCTRCTCQLGEVSCEKVPCQRACA
551
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        670 CTYPFHPDGECCPVCRDCNYEGRKVANGQVFTLDDEPCTRCTCQLGEVSCEKVPCQRACA
729

Qy        552 DPALLPGDCCSSCPDSLSPLEEKQGLSPHGNVAFSKAGRSLHGDTEAPVNCSSCPGPPTA
611
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        730 DPALLPGDCCSSCPDSLSPLEEKQGLSPHGNVAFSKAGRSLHGDTEAPVNCSSCPGPPTA
789

Qy        612 SPSRPVLHLLQLLLRTNLMKTQTLPTSPAGAHGPHSLALGLTATFPGEPGASPRLSPGPS
671
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        790 SPSRPVLHLLQLLLRTNLMKTQTLPTSPAGAHGPHSLALGLTATFPGEPGASPRLSPGPS
849

Qy        672 TPPGAPTLPLASPGAPQPPPVTPERSFSASGAQIVSRWPPLPGTLLTEASALSMMDPSPS
731
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        850 TPPGAPTLPLASPGAPQPPPVTPERSFSASGAQIVSRWPPLPGTLLTEASALSMMDPSPS
909

Qy        732 KTPITLLGPRVLSPTTSRLSTALAATTHPGPQQPPVGASRGEESTM 777
              ||||||||||||||||||||||||||||||||||||||||||||||
Db        910 KTPITLLGPRVLSPTTSRLSTALAATTHPGPQQPPVGASRGEESTM 955
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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 63 and 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isogai et al. (U.S. Patent No. 6,979,557) in view of Godbole et al. (US Patent Publication 2003/0100746).

Isogai et al. is applied as above but does not disclose methods of treatment.

Godbole et al. discloses using fibulin proteins to promote bone and cartilage regeneration in methods of treatment. See at least pages 22 and 25.

It would have been obvious to use the fibulin protein of Isogai et al. in the method of treatment disclosed by Godbole et al. One would have been motivated to do so to provide additional therapies to treat these conditions.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is (571)272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

mpa